Acid-Catalyzed Conversion of Epoxyesters to Hydroxyesters[1]

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Abstract

Esters of 9,10-epoxystearic acid (epoxidized oleic acid), dissolved in 1,4-dioxane, were treated at 15C, first with aqueous acid and then with water to convert them to 9,10-dihydroxystearates in high yields. Ester functions remained intact. Glycidyl 9,10-epoxystearate, ethylene glycol *bis*-9,10-epoxystearate and catechol *bis*-9,10-epoxystearate were converted to the corresponding tetrahydroxy esters by this method.

Treatment of methyl 9,10-epoxystearate with diluted (24%) fluoboric acid gave methyl 9,10-dihydroxystearate in 89% yield. Under similar conditions glycidyl stearate did not react and the internal epoxy group of glycidyl 9,10-epoxystearate was hydrated preferentially.

Hydration of methyl 9,10-epoxystearate with concd H_2SO_4 led to the formation of considerable amt of byproducts, principally methyl 9(10)-ketostearate. Side reactions were inhibited by diluting the acid-catalyst.

Introduction

RECENTLY (1) we reported a procedure by which glycidyl stearate, an ester having a terminal epoxy group, is converted to monostearin, an ester containing a vicinal glycol group, in high yield. Ester hydrolysis, which constitutes an undesirable side reaction occurring in aqueous acid medium at elevated temp, is avoided by effecting the hydration with the aid of a strong acid in non-aqueous solvent at room temp or below. The path of this reaction is not known with certainty, but some experimental findings in our work were consistent with the hypothesis that the ester carbonyl group aided in the opening of the epoxide ring, at least part of the time.

The present work is concerned with the hydration of epoxy esters in which the oxirane function is located internally along the hydrocarbon chain of the acid portion. As a model compound we chose to study methyl 9,10-epoxystearate, a readily available compound which is representative of materials found in many epoxidized natural oils. In this compound, assistance of the ester carbonyl group in epoxide ring opening is quite unlikely, since the two functional groups are separated by seven methylene groups. Furthermore, it is well known that the reactivity of internal epoxides toward various chemical reagents differs considerably from that of terminal oxiranes. We were therefore interested in comparing the hydration conditions required for methyl epoxystearate with those demanded by glycidyl stearate.

Nishiyama et al. (2) have studied the hydration of butyl 9,10-epoxystearate and of the butyl esters of epoxy soybean fatty acids both in heterogeneous and in homogeneous (acetone) media. Their work, which was concerned mainly with rates of epoxide consumption rather than with a study of the products formed, is complemented by ours to a certain extent. A direct comparison of results, however, is not possible.

We studied the hydration of methyl 9,10-epoxystearate dissolved in dioxane, using both H_2SO_4 and fluoboric acid as catalysts. The latter acid was also employed to prepare polyhydroxy derivatives of glycidyl 9,10-epoxystearate, ethylene glycol *bis*-9,10-epoxystearate and catechol *bis*-9,10-epoxystearate. Along with the desired alcohols, we obtained byproducts stemming from the acid-catalyzed rearrangement or polymerization of the oxirane function. The extent of this byproduct formation varied with hydration conditions.

Experimental Procedures and Data

Materials Used

Methyl 9,10-Epoxystearate. This compound was prepared by epoxidation of methyl oleate (3). Oxirane oxygen (4): 5.01%, theory 5.12%. Thin-layer chromatography (TLC) and gas-liquid chromatography confirmed a purity of approximately 98–99%.

Glycidyl 9,10-Epoxystearate. To 41.7 g 9,10-epoxystearic acid (oxirane: 5.09%, theory 5.36%) dissolved in 700 ml acetone was added dropwise 5.3 g sodium hydroxide in 16 ml water with vigorous stirring. Addition time 1.5 hr at 25–30C. The resulting slurry was agitated at 25–30C for an additional 3 hr and filtered. The cake was triturated with 200 ml acetone, filtered and dried to give 40.0 g sodium 9,10-epoxystearate, A.N: 1.7, specific acid number ($\overline{N}_A$) (5): 0.029. Analysis by HBr in acetic acid by a modification of the Durbetaki method (4) gave an "oxirane content" of 9.37%. The theoretical oxirane content for this compound is 9.98% since both the oxirane oxygen and the sodium ion are titrated by HBr under these conditions (6).

Sodium 9,10-epoxystearate (32.0 g) and redistilled epichlorohydrin (148.0 g) were heated to reflux and benzyltrimethylammonium chloride (3.7 g) was added. The reaction mixture was refluxed 20 min, cooled and washed twice with 150 ml water. Unreacted epichlorohydrin was removed by distillation at 6 mm under a stream of N_2. Toluene was added and distillation repeated. Obtained 36.0 g (82.9% yield based on 9,10-epoxystearic acid) glycidyl 9,10-epoxystearate, oxirane content: 7.85% (theory: 9.03%). The ester was further purified to an oxirane content of 8.66% by chromatography on silica gel.

Ethylene Glycol bis-9,10-Epoxystearate. The material prepared by Gelb et al. (7) was recrystallized from methanol. Oxirane: 4.99% (theory: 5.15%).

Catechol bis-9,10-Epoxystearate. Material prepared by Port and Komanowsky (8) was used. Oxirane: 4.69% (theory: 4.77%).

1,4-Dioxane. 1,4-Dioxane (Eastman-practical) was purified according to the method of Hess and Frahm (9).

Fluoboric Acid. Fluoboric acid, purified, 48–50% (J. T. Baker Chemical Co.) was used as received.

Procedures

Hydration of Methyl 9,10-Epoxystearate. The following example is typical of the procedure employed. Data resulting from variations in this procedure show in Tables I and II.

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TABLE I

Hydration of Methyl 9,10-Epoxystearate with HBF_4

HBF_4 concn %	Yield (%) in crude product		
	Methyl 9,10-epoxy-stearate	Methyl 9(10)-keto-stearate	Methyl 9,10-dihydroxy-stearate
16	4.0	2.4	86.0
24	6.2	5.3	89.0
48	....	26.0	65.0

TABLE II

Hydration of Methyl 9,10-Epoxystearate with H_2SO_4

H_2SO_4 concn %	Composition (%) of crude product			
	Methyl 9,10-epoxy-stearate	Methyl 9(10)-keto-stearate	Methyl 9,10-dihydroxy-stearate	Other compounds
65	7.0	5.0	46.0	42.0
95	7.0	15.0	28.0	50.0
100	4.0	40.0	27.0	29.0

A solution of 5.0 g methyl 9,10-epoxystearate (98% pure) in 60 ml 1,4-dioxane was cooled with stirring to 15C. To this solution was added dropwise over a period of 3 min a solution of 4.8 g commercial fluoboric acid in a mixture of 4.8 g water and 15 ml dioxane while the temp of the reaction mixture was held at 15 ± 1C. After acid addition was complete, the reaction mixture was agitated for 35 min at 15 ± 1C. The addition of 10 ml water was followed by an agitation period (10 min) at 15 ± 1C. Throughout this procedure the mixture remained clear and water white. The mixture was poured into 150 ml benzene, the aqueous acid phase was withdrawn and the benzene solution was washed successively with 25 ml aqueous sodium bicarbonate (5%) and with three 50 ml portions of water. The benzene solution was dried over Drierite and evaporated under nitrogen to a slightly yellow, solid residue, 5.13 g, oxirane: ~0.3%.

Chromatography of 1 g of the crude glycol on silica gel (Davison #923) gave 0.11 g methyl 9(10)ketostearate mixed with a small amt of methyl 9,10-epoxystearate and 0.89 g methyl 9,10-dihydroxystearate. The latter was recrystallized from Skellysolve B to pure methyl 9,10-dihydroxystearate, mp 68.0–68.8C [lit. (10): 70C].

Hydration of Glycidyl 9,10-Epoxystearate. A solution of 4.87 g glycidyl 9,10-epoxystearate (98.6% pure) in 60 ml 1,4-dioxane was cooled to 15C and treated with a solution of 10.0 g HBF_4 in a mixture of 10.0 g H_2O and 20 ml 1,4-dioxane in the manner described for the hydration of the methyl ester. Evaporation of the benzene solution gave 4.68 g residue, oxirane: 2.95%. IR spectra and the characteristic fading endpoint in the HBr oxirane analysis indicated that virtually all of the remaining oxirane groups were in the terminal position, i.e., in the alcohol portion of the ester.

The partially hydrated ester (4.48 g) dissolved in 65 ml 1,4-dioxane was now treated with 5.0 g HBF_4 in 15 ml dioxane (no water added) at 15C for 10 min, and the mixture treated with water and worked up in the usual manner. Evaporation of the benzene solvent gave 4.0 g residue, oxirane: 0.9%, mp 71.5–75.5C. Two recrystallizations from benzene gave glyceryl 9, 10-dihydroxystearate, mp 80.5–81.5C.

Anal. Calc'd for $C_{21}H_{42}O_6$: C, 64.58; H, 10.84; OH, 17.42.

Found: C, 64.79; H, 11.02; OH, 17.43.

Hydration of Catechol bis-9,10-Epoxystearate. A solution of 5.0 g catechol *bis*-9,10-epoxystearate (98.3% pure) in 90 ml 1,4-dioxane was cooled to 13C. A solution of 5.0 g HBF_4 in a mixture of 5.0 g H_2O and 15 ml dioxane was added at 13–14C over a period of 10 min and stirring continued for 20 min. Water (10 ml) was added at a fast dropwise rate (1 min) and the mixture was stirred for an additional 10 min at 13–15C. The resulting slurry was poured into benzene, and the aqueous acid layer was withdrawn. The remaining organic layer, which contained a suspended, crystalline solid, was washed successively with 50 ml H_2O, 50 ml $NaHCO_3$ solution (5%) and 2 x 50 ml H_2O. The suspension was then filtered and the cake dried (A, 1.25 g, mp 100.5–104.0C). The benzene filtrate was dried over Drierite and evaporated to a solid residue (B, 3.61 g, mp 87–90C, oxirane oxygen: 0.37%).

The IR spectrum of solid A indicated that it was impure catechol *bis*-9,10-dihydroxystearate. One crystallization from toluene at room temp and two recrystallizations from chloroform at 2C gave catechol *bis*-9,10-dihydroxystearate, mp 110.1–110.9C.

Anal. Calc'd for $C_{42}H_{74}O_8$: C, 71.35; H, 10.55; OH. 9.62.

Found: C, 71.69; H, 10.62; OH, 9.70.

The IR spectrum of solid B indicated that it also was impure catechol *bis*-9,10-dihyroxystearate. The solid was extracted with Skellysolve B, and the insoluble residue was crystallized once from toluene at room temp and twice from chloroform at −30C (no crystals formed at 2C) to obtain catechol *bis*-9,10-dihydroxystearate, mp 96.1–98.0C.

Anal. Calc'd for $C_{42}H_{74}O_8$: C, 71.35; H, 10.55; OH. 9.62.

Found: C, 71.61; H, 10.98; OH, 9.55.

X-Ray powder spectroscopy studies indicated that the high melting compound (long spacing, 47.9 Å) and the low melting compound (long spacing 50.1 Å) have different patterns and could be optical isomers.

Hydration of Ethylene Glycol bis-9,10-Epoxystearate. To a solution of ethylene glycol *bis*-9,10-epoxystearate in 85 ml 1,4-dioxane cooled to 15C was added a solution of 5.0 g HBF_4 in a mixture of 10.0 g H_2O and 15 ml dioxane. Addition time 7 min. Two minutes after start of acid addition solids started to separate and the solution soon became a slurry. The reaction mixture was allowed to warm to 20C during the balance of the acid addition in an attempt to improve contact among reagents. After completed addition, agitation was continued for 40 min while the temp rose to 26C. At the end of this period, 10 ml H_2O was added in 1 min and stirring continued for 9 min. The slurry was poured into 150 ml $CHCl_3$ (all solids dissolved), and the aqueous acid layer was drawn off. The organic solution was worked up in the usual manner and upon evaporation gave 4.89 g residue, mp 97.5–104.5C, oxirane: 0.13%. TLC showed a single principal component and four byproducts.

Column chromatography on silica gel (Davison #923) indicated that the crude product was composed of the following ethylene glycol esters (percentages estimated from IR spectra): *bis*-dihydroxystearate 79%, ketostearate-dihydroxystearate 18%, ketostearate-epoxystearate 1%, *bis*-epoxystearate 2%. The major component eluted from the column was recrystallized from benzene to give ethylene glycol *bis*-9,10-dihydroxystearate, mp 101.5–106.2C.

Anal. Calc'd for $C_{38}H_{74}O_8$: C, 69.26; H, 11.32; OH, 10.32; Sap. Equiv., 329.5.

Found: C, 69.70; H, 11.66; OH, 10.70; Sap. Equiv., 328.9.

Recrystallization of this ester from acetone gave a solid, mp 101.7–102.0C. Recrystallization of a portion of the latter solid from toluene gave the original product, mp 101.5–106.5C. The two solids, one having a sharp melting point and the other a diffuse, slightly higher melting point, were examined by X-ray powder spectroscopy which indicated the probability that the two solids are polymorphs.

Results

Previous studies (1) had demonstrated that 1,4-dioxane is an excellent solvent for the hydration reaction, and this solvent was therefore used exclusively for the present investigation. The two-step hydration procedure, adopted in our earlier work and consisting of a protonation step followed by a hydration step, was retained for the current work, particularly since we were interested in comparing the behavior of terminal oxirane groups with that of internally located groups and thus link previous work with our present studies.

The data assembled in Table I indicate that diluted (24%) fluoboric acid is considerably more effective in giving high yields of the desired glycol than is the commercial (48–50%) strength acid. The effect of the same hydration conditions upon glycidyl stearate is quite different. The diluted (24%) acid does not attack glycidyl stearate to any significant extent, and more than 90% of the unchanged starting material can be recovered after the normal reaction period. On the other hand, 48% HBF_4 converts the glycidyl ester to the monoglyceride in 91% yield. These results would seem to indicate that location of the oxirane function influences hydration requirements distinctly, although the extent of this influence is not determined readily. Most likely the proximity of the ester carbonyl group in glycidyl esters also affects the ease with which the oxirane groups of these compounds are hydrated.

In this connection it is interesting to note the behavior of phenyl glycidyl ether when subjected to the hydration reaction. Under standard hydration conditions 56% of this compound remained unreacted when 24% HBF_4 was the catalyst, while 16% did not react with 48% HBF_4. Rearrangement of the epoxide to aldehyde or ketone was not observed in either case.

The failure of the higher strength acid to give good yields of methyl 9,10-dihydroxystearate is apparently due to its inability to suppress competing acid-catalyzed reaction of the internal epoxide group, particularly isomerization to the ketone. The presence of greater amt of water during the protonation step seems to inhibit byproduct formation to a point. However, addition of even more water during the protonation step, i.e., use of 16% HBF_4 as catalyst, does not increase the yield of 9,10-dihydroxystearate further.

The difference between glycidyl and internal epoxy esters in their response toward 24% and 48% HBF_4 was further tested by combining both types of oxiranes in a single ester, glycidyl 9,10-epoxystearate. Hydration of this compound with 24% HBF_4 showed a definite preference for attack at the internal epoxide group. Completion of the reaction, i.e., formation of the tetrahydroxy ester, required use of 48% acid.

Byproduct formation increased when H_2SO_4, rather than fluoboric acid, was used in the hydration of methyl 9,10-epoxystearate (see Table II). Both acids give greater yields of glycol and lesser amt of isomerization products (ketostearate) when diluted with water, but H_2SO_4 also gives rise to considerable quantities of other byproducts which were not observed when fluoboric acid was the catalyst. The nature of some of the principal components of these byproducts are presently being investigated.

Hydration of esters of diepoxides having both epoxy groups on the same hydrocarbon chain, e.g., methyl 9,10,12,13-diepoxystearate, leads to abnormal products, and the nature of these products is the subject of a current study. It was therefore of interest to determine whether epoxy groups on adjacent chains give the expected hydration products. Ethylene glycol *bis*-9,10-epoxystearate and catechol *bis*-9,10-epoxystearate both hydrated normally with 24% HBF_4, and no interaction between oxirane groups on adjacent chains could be discovered. The only byproducts found were those in which one of the epoxy groups had isomerized to ketone.

The stereochemistry of the conversion of internal epoxides to the corresponding glycols deserves brief consideration. Monoepoxides such as methyl 9,10-epoxystearate are normally obtained as racemic mixtures of *d* and *l* isomers. The latter arise and are formed in equal amt, because the epoxidizing agent may approach the planar double bond from either side with equal probability. Hydration of the epoxide function is a two-step reaction (11) in which the initial protonation of the oxygen is followed by the nucleophilic attack by a molecule of water at the rear of one of the carbon atoms of the epoxide group. Formation of the glycol, then, results in breakage of one carbon-oxygen bond and formation of a new carbon-oxygen bond with inversion of configuration at the carbon attacked. Thus *cis*-epoxides should be hydrated to *threo*-glycols and *trans*-epoxides to *erythro*-glycols. In the absence of controlling stereochemical or electronic factors, attack at either carbon atom is equally probable, and a racemic mixture of vicinal glycols is actually produced. Furthermore, each of two enantiomorphic epoxides gives rise to the same pair of glycols so that the net result is that an inactive racemic mixture of epoxides is hydrated to an inactive, racemic mixture of vicinal glycols.

In line with these considerations, it is expected that acid-catalyzed hydration converts methyl 9,10-epoxystearate to methyl *threo*-9,10-dihydroxystearate. The product isolated experimentally was indeed the lower-melting, *dl-threo*, ester.

The *bis*-9,10-epoxystearate esters of ethylene glycol and of catechol are symmetrical molecules which contain two oxirane functions. Hydration converts each oxirane group independently to either the *d-threo* or the *l-threo* glycol, regardless of the configuration of the intial *cis*-epoxide. Since the two ends of the molecule are identical, the tetrahydroxy esters produced will be internally compensated inactive (*meso*) isomers if the two *threo* glycol groups rotate light in opposite directions, or they will be inactive mixtures of active (*dl*) isomers if both *threo* glycol functions in the same molecule have identical rotational direction. The situation is illustrated schematically in Figure 1, where the small triangles represent oxirane groups and the rectangles depict the central portions of the molecule.

Hydration of catechol *bis*-9,10-epoxystearate produced two products which gave the correct analysis for catechol *bis*-9,10-dihydroxystearate. The two materials, one melting at 96.1–98.0C after crystallization from chloroform at −30C, and the other melting at 110.1–110.9C after crystallization from chloroform at

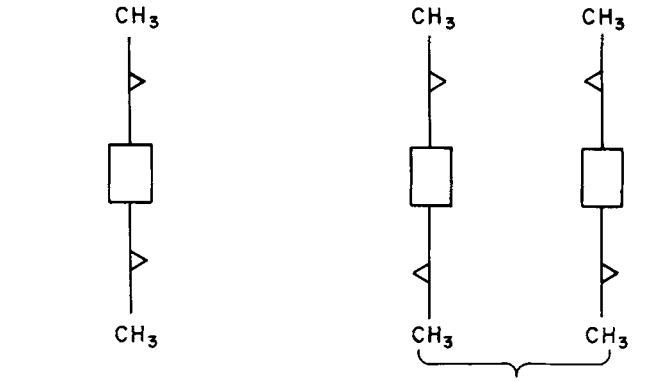

FIG. 1.

2C presumably are the expected *meso* isomer and the racemic mixture, but further work is required to make a definite configurational assignment.

Ethylene glycol *bis*-9,10-dihydroxystearate was also obtained as two solid forms. One solid, crystallized from acetone, melted at 101.7–102.0C, while the other crystallized from toluene, melted diffusely at 101.5–106.5C. Since these two materials are interconvertible so that their melting point is a function of the crystallization solvent, they are believed to be polymorphic forms of the same optical isomers, either the *meso* form or the *dl*-mixture. The expected second isomer was not isolated.

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Analysis of Triglycerides by Consecutive Chromatographic Techniques. I. *Cuphea llavia* Seed Fat[1]

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Abstract

The triglycerides of *Cuphea llavia* var. *miniata* seed fat were separated according to the number of double bonds/molecule using preparative thin layer chromatography (TLC) on silicic acid impregnated with silver ion. The recovered fractions were quantitated by the chromotropic acid technique. Each fraction was then separated according to mol wt using gas-liquid chromatography (GLC). This multiple chromatography procedure resolved *C. llavia* triglycerides into 17 different components.

The triglyceride composition of *C. llavia* seed fat was calculated from the above results. Since the fat contains 91.2 mole % decanoic acid, it was expected that each triglyceride molecule would contain at least two molecules of decanoic acid. Results showed this to be generally true, but several minor component triglycerides not conforming to this pattern were found.

Introduction

THE PAST FIVE YEARS have been exciting times in the search for new analytical techniques for determining the triglyceride composition of natural fats. Techniques recently introduced in this field have included: pancreatic lipase hydrolysis (1,2), silver ion (Ag^+) chromatography (3,4), GLC (5,6), liquid-liquid partition chromatography (7,8,9), and various chromatographic methods for separating oxidized triglycerides (10,11).

The triglyceride compositions of most natural fats are so complex that no one analytical technique can completely resolve all components. Until recently, most workers have utilized only one separation method to study natural triglyceride mixtures. Considerably more information can be obtained, however, by the successive application of several separation techniques to natural triglycerides. For example, Youngs (10) has used permanganate-periodate oxidation on a number of fats and then analyzed the resultant triglyceride "cores" by liquid-liquid partition chromatography and lipase hydrolysis. Privett and Blank (11) have separated triglyceride ozonides by adsorption chromatography and then rechromatographed each hydrogenated fraction by the same method.

The present work was undertaken to demonstrate how a combination of Ag^+ chromatography and GLC can be used to characterize the triglyceride composition of *Cuphea llavia* seed fat. Triglycerides were first separated according to the number of double bonds/molecule using Ag^+ chromatography. The recovered fractions were then analyzed by GLC to determine the mol wt of the triglycerides present. The triglyceride composition of the total fat was then calculated from these results.

Cuphea llavia var. *miniata* (also known as *Cuphea miniata* var. *firefly*) is a subtropical ornamental shrub cultivated in the southern United States where it is commonly called the "Mexican cigar flower." The fatty acid composition of *C. llavia* seed fat has been investigated by Earle et al. (12) and found to contain 83 wt % decanoic acid. The triglyceride composition of this fat has not been previously reported.

Procedures

Materials

Cuphea llavia var. *miniata* seeds (Thompson & Morgan, Ipswich, England) were sorted to remove damaged seeds and foreign material. 11.58 g cleaned

[1] Presented at the AOCS Meeting in Minneapolis, 1963.